Remarks

The above amendment to claim 1 is supported by the specification as originally filed, for example, at page 15, lines 13-19; page 17, lines 1-2; page 18, lines 19-20. Support for new claim 17 is found in the specification, for example, at page 4, line 29 through page 5, line 5. No new matter has been added. Claims 1-4, 6-11, and 13-17 remain pending in this application. Reconsideration is respectfully requested in view of the above amendments and following remarks.

Rejection under 35 USC 103

Claims 1-4, 6-11, and 13-16 remain rejected as allegedly being obvious over Hajek et al. in view of Fodstad et al. and O'Briant et al. Applicants respectfully traverse the rejection.

Regarding the suggestion that flow cytometry could be used with the claimed method, Applicants submit the enclosed declaration by the inventor, showing that no results are obtained when flow cytometry is used with the claimed method.

The Examiner asserts that it would have been obvious to use a cell suspension, as taught by Fodstad et al. rather than a smear sample on a slide, as taught by Hajek, et al. for visualization under the microscope because they are interchangeable and well known methods in the art. However, Hajek et al. specifically teach that rimming, or clumping occurs in the cell suspension when cells are positive for an antigen (see column 12, lines 17-36). The cell clumping is not a problem in the method of Hajek et al. because they teach smearing the cells on a slide, drying, and staining the cells. Making a smear of the cells would disrupt the clumps and allow the individual cells to be visualized (see Figure 4). While some cells are close together and covered with microspheres, the individual cells can still be seen, and the color and/or size of the microspheres can be determined to allow proper analysis. Thus, the agglutination does not interfere with the identification in Hajek et al.

However, the instant method requires analyzing the cells in suspension, not smeared on a slide. Clumping of cells and particles would interfere with the analysis since the individual cells would be obscured by the cell-particle clumps. Additionally, since the instant invention requires 2 to 6 different antibody-particle conjugates, with many of the antibodies binding the same cells, one would expect significant clumping and/or steric hindrance to occur, thus interfering with the suspension analysis. The instant specification teaches that surprisingly "mixed cell populations

could be incubated simultaneously, or subsequently, with a number of different particle-bound antibodies...and that the binding of different complexes could easily be visualized and distinguished in a fluorescence microscope" (see page 13, lines 4-12).

Applicants submit that one of ordinary skill in the art would not have been motivated to analyze a suspension of Hajek et al. instead of a smear Hajek et al. teach that the suspension clumps. Additionally, one would not have a reasonable expectation of success in substituting a suspension analysis for the smear analysis because the clumping described by Hajek et al. would be expected to interfere with visualizing the cells. There is no motivation to combine the teachings of Hajek et al. and Fodstad et al., and no expectation of success in such combination if one were made.

O'Briant et al. merely teaches immunomagnetic separation of tumor cells from a cell mixture, and thus does not provide any motive for combining the teachings of Hajek et. al. and Fodstad et al. Because there is no motivation to combine the references, and no expectation of success in making such a combination, withdrawal of the rejection is respectfully requested.

Conclusion

With the above amendments and remarks, Applicants believe that the claims now pending in this patent application are in a condition for allowance. Favorable consideration is respectfully requested. If any further questions arise, the Examiner is invited to contact Applicants' representative at the number listed below.

Respectfully submitted,

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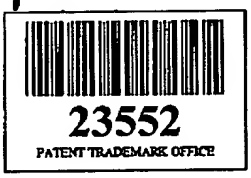

MARKED-UP VERSION TO SHOW CHANGES MADE

1. (Thrice Amended) Method to detect and phenotype target cells in cell suspensions by using particles coated with antibodies directed against antigenic determinants/receptors expressed on the target cells, wherein 2 to 6 antibodies, each conjugated to a particle, wherein the particle is a fluorescent or dyed particle, are incubated under gentle rotation for about 5 minutes to about 2 hours with cell suspensions containing the target cells at 0°C to 25°C, followed by an enrichment procedure, and evaluation of the target cell rosettes microscopically and/or by suitable visualizing or imaging devices, wherein the cells are evaluated while in suspension, and wherein one antibody is conjugated to one type of particle instrumentally or visually separable by fluorescence, color and size, with sizes of the particles ranging from 0.01μm to 6μm, each antibody of the 2 to 6 antibodies is conjugated to different particles, and the ratio between the number of particles and the number of cells ranges from 0.5 : 1 to 20 : 1 in the cell suspension.

2. (Twice Amended) Method according to claim 1, wherein the [the] said size of the particles ranges from about 0.5μm to about 4.5μm, the said ratio is 5 :1 (number of particles/number of cells), the said incubation time is 30 minutes and the said incubation temperature is 4 ° C.

10. (Twice Amended) Method according to claim 9, wherein [the] target cell characteristics of biologically informative markers of diagnostic, prognostic and therapeutic value are registered.

13. (Twice Amended) Method according to claim 10, wherein the biologically informative markers are E-cadherin, EGFr, c-erbB2, IL-2 receptor, TNF receptor , EGP2, MUC1, MUC2 & 3, PSA, PSM, GA733.2, TAG72, 15-3 epitope, ovarian carcinoma CA- 125 epitope, Le^y, CEA, 15-3 epitope, HMW 250000 melanoma antigen, gp 75/TRP-1, p95, MAG 1, MAG 2, MAG 3, TP 1 and TP 3 eptiopes, Mel-14 epitope, Fas, FasL, p75, KAT-1, AMF, gp120, MUC 18, TA99, MDR, MRP, VEGFr, bFGF, CCR, CXCR, uPAR, uPA, PAI-1, TIMP1 & 2, MMP9, stromelysins, and cathepsin D and par-human epitope.